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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/772,116	01/26/2001	Howard Benjamin	PPI-012CN	9135

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LAHIVE & COCKFIELD, LLP.
28 STATE STREET
BOSTON, MA 02109

EXAMINER	
PONNALURI, PADMASHRI	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 11/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/772,116	BENJAMIN ET AL.	
	Examiner	Art Unit	
	Padmashri Ponnaluri	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 10-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7, 10-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The response filed on 9/8/05 has been fully considered and entered into the application.

2. Claims 1-7 and 10-23 are currently pending in this application.

Priority

3. This application is a continuation of application 08/573,786, filed on 12/18/95.

Withdrawn Claim Rejections

4. The indefiniteness rejection of claims 1-7, 10-23 over the term 'family of peptides' has been withdrawn in view of the response.

5. The lack of utility rejection of claims1-7, 10-23 under 35 U.S.C. 101, set forth in the previous office action, has been withdrawn in view of the applicant's response.

Maintained Claim Rejections

6. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

7. The new matter rejection of claims 1-7, 10-23 under 35 U.S.C. 112, first paragraph, for the reasons set forth in the previous office action mailed on 3/8/05 has been maintained.

8. The lack of written description rejection of claims 1-7, 10-23 under 35 U.S.C. 112, first Paragraph set forth in the previous office action mailed on 3/8/05 has been maintained for the reasons of record.

9. The obviousness rejection of claims 1-3, 5-7, 10-16, 21-23 over Lam et al and Gallop et al, set forth in the previous office action mailed on 3/8/05 has been maintained for the reasons of record.

10. The obviousness rejection of claims 1-7, 10-16, 21-23 over Lam et al and Gallop et al, and Benjamin et al set forth in the previous office action mailed on 3/8/05 has been maintained for the reasons of record.

The obviousness rejection of claims 1-7, 10-16, 21-23 over Lam et al and Gallop et al, and Stankova et al (Drug Development Research, vol. 33, pages 146-156, 1994), set forth in the previous office action mailed on 3/8/05 has been maintained for the reasons of record.

The provisional obviousness-type double patenting rejection of claims 1-7, 10-23 over claims 1-33 of copending Application No. 10/610,927, set forth in the previous office action mailed on 3/8/05 has been maintained for the reasons of record.

Response to Arguments

11. Claims 1-7, 10-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The limitation 'a family of peptides that bind to the target' claimed in claims 1, 22-23 has no clear support in the specification and the claims as originally filed. The specification discloses 'once the peptide library is formed, a target of interest is screened with the peptide library to identify one or more library members that bind to target... ' The subject matter claimed in claims 1, 22-23 broadens and/or alters the scope of the invention as originally disclosed in the specification.

If applicants disagree, applicant should present a detailed analysis as to why the claimed subject matter has clear support in the specification.

12. Applicant's arguments filed on 9/8/05, regarding the new matter rejection have been fully considered but they are not persuasive.

Applicants traverse the rejection. Applicants assert that the specification has support for the limitation 'family of peptides that bind to the target.' Applicants assert that 'family of peptides' is an art recognized term that is supported in the specification in page 12, lines 24-27.

Applicant's assertions have been considered and are not persuasive, since the rejection is set forth as 'new matter rejection' and the limitation have no support in the instant specification.

Applicants arguments that the term 'art recognized term' does not support the term and do not overcome the rejection. Further, applicants point out that specification page 12, lines 24-27, has support for the 'family of peptides' is not persuasive. Because the specification page 12, lines 24-27 refers to the 'LHRH-R as a member of the G-protein coupled, seven transmembrane receptor superfamily.' The specification no where teaches that a family of peptides that bind to a target from the first library.

Applicant's response has addressed 'the new matter rejection' set forth as written description rejection. Applicants argue that 'applicants use do the term 'family of peptides that bind to target' is both art recognized term and adequately supported by the specification.

Applicants arguments are not persuasive, since the term 'family of peptides' is art recognized term, but the use of the term in the claimed method has no support in the specification as originally filed. The specification has not taught the 'selecting from the first library a family of peptides that bind the target'; and 'determining the amino acid sequence of the family of peptides that bind to target from the first library.'

13. Claims 1-7, 10-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s),

at the time the application was filed, had possession of the claimed invention. This is written description rejection.

The instant claims briefly recite a method for identifying a non-peptide compound that binds to a target, the method comprising: a) forming a first library of peptides; b) selecting from the first library a family of peptides that bind to the target; c) determining the amino acid sequence of the family of peptides and generating a peptide motif; d) forming a second library comprising non-peptide compounds; e) selecting from the second library at lest one-non-peptide compounds that bind to the target; f) determining the structure of at least one non-peptide compound; g) thereby identifying the non-peptide compounds that binds the target.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406. A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Although directed to DNA compounds, this holding would be deemed to be applicable to any compound; which requires a representative sample of compounds and/or a showing of sufficient identifying characteristics; to demonstrate possession of the claimed generic(s).

The instant specification disclosed general, well-known peptide synthesis methods. The specification further discloses narrative, hypothetical methods of generating peptide libraries and identifying the active compound from the library and use the compound to generate peptide analogue libraries (second libraries), and screening the peptide analogue library for a ligand which binds the target. The specification discloses that the first peptide library is screened with a target, and once the sequences of peptides that bind to the target is selected, a 'peptide motif' is generated. The specification discloses that the peptide motif for the target of interest, a second non-peptide library based on the peptide motif is generated. The specification discloses second library comprising analog library or the second library is synthesized based on altering D and L-amino acids; or the second library synthesized based on introduction of peptide mimetics at one or two positions within the library.

The specification has not disclosed the structure of the non-peptides of the second library or the non-peptides compounds, which bind to target and has binding affinity of at least 10^{-7} M, 10^{-8} M or 10^{-9} M.

The working example of the specification are drawn to construction of phage library (first library) comprising sixteen amino acids length and have amino acid sequence of SEQ ID NO: 1; screening the first library with LHRH-R, and from the selected peptides, SEQ ID NO: 6 is determined as the peptide motif of interest; based on the peptide motif a second library which is analog library or a mimetic library; screening the second library to identify members which bind to LHRH-R. The specification has not disclosed the non-peptides generated using the peptide motif of SEQ ID NO: 6, and has not disclosed the binding affinity of the non-peptides generated based on the peptide motif of SEQ ID NO: 6 to the LHRH-R (target).

The specification has not disclosed how the peptide motif is derivatized or substituted to obtain the peptide mimetics, or the analogues. The specification has not disclosed the structure of the non-peptides. The specification has not disclosed the use of the non-peptide compounds identified from the second library. The working example in the specification does not disclose the non-peptides, and whether the identified non-peptide is used in any other methods. The specification discloses that the identified non-peptide from the second library can be used to generate a third library.

The specification disclosure is hypothetical, and does not disclose the length of the peptide library or the position of modifications or substitutions of the peptide motif to generate the second library, or the number of modifications in the peptide motif or the target used. The specification disclosed hypothetical method, which requires to identify the peptides in a library that bind to the target, and then further methods of generating a peptide motif, which is specific to the target, and then further use of the peptide motif in generating second non-peptide library. The working example in the specification is drawn to a single species of specific peptide motif and method of generating a second non-peptide library. However, the working examples do not disclose the non-peptide identified by the claimed method, and/or the structure of the non-peptide compound identified.

And further the claimed method depends upon finding a peptide or family of peptides that selectively bind to a target, and generating a peptide motif specific to the target and further use of thus generated peptide motif to generate a non-peptide (or analogue) library and further screening the non-peptide library for members which bind to the target. Thus, applicants are not in possession of the peptide members, which bind to the target, and peptide motif and the non-peptides, and it would be impossible to practice the claimed method, since applicants are not in possession of the compounds, which are essential to practice the claimed method.

Further the specification disclosure of second library comprising non-peptide compounds clearly do not provide an adequate representation regarding the open ended claimed non-peptide library

compounds made and screened by the presently claimed invention. The instant claim non-peptide compounds would read on peptide derivatives, peptidomimetics or peptide analogues, or small organic molecule compounds which specification has no written support.

In the present instance, the claimed method contains no identifying characteristics regarding the peptide members identified (from the first library) or the peptide motif, or the non-peptide compounds of the second library.

Additionally, the narrow scope of example is directed to one single peptide of 16 amino acids in length, which binds to LHRH-R, and method of generating peptide analogs or peptidomimetic compounds, clearly not representative of the scope of the presently claimed invention.

14. Applicant's arguments filed on 9/8/05, regarding the lack of written description rejection, have been fully considered but they are not persuasive.

Applicants traverse the rejection. Applicants assert that the claimed method is directed to Screening methods and not the compounds that are identified by these screening methods.

Applicant's assertions have been fully considered, and are not persuasive. Applicants seem to be asserting that 'the lack written description rejection is only applicable to compounds per se, and not to the methods.' Applicant's arguments and assertions have been fully considered and are not persuasive.

Written description requirement of 35 USC. 112 exists independently of enablement requirement, and the requirement applies whether or not case involves question of priority, ***since requirement applies to all inventions including chemical inventions, and since the fact that patent is directed to method entailing use of compound, rather than to compound perse, does not remove patentee's obligation to provide description of compound sufficient to distinguish***

infringing methods from non-infringing methods. *See Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 920-23, 69 USPQ2d 1886, 1890-93 (Fed. Cir.2004).*

Applicants assert that the specification contains ample description of the claimed method, and contains working examples describing the claimed method.

Applicant's assertions have been considered and are not persuasive.

The working example of the specification is drawn to specific peptide of specific length (sixteen amino acids) and specific sequence (SEQ ID NO: 1); screening the first library with LHRH-R, and from the selected peptides, SEQ ID NO: 6 is determined as the peptide motif of interest; based on the peptide motif a second library which is analog library or a mimetic library; screening the second library to identify members which bind to LHRH-R. The specification has not disclosed the non-peptides generated using the peptide motif of SEQ ID NO: 6, and has not disclosed the binding affinity of the non-peptides generated based on the peptide motif of SEQ ID NO: 6 to the LHRH-R (target).

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.

A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation

within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. See MPEP 2163.

In this case the description of 'specific peptide library and screening the peptide library with a specific target (LHRH-R), and then identified motif (SEQ ID NO:6) used in construction of second analog library (of D-amino acids)' is not representative of the claimed broad method of identifying non-peptide compounds.

15. Claims 1-7, 10-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-7, 10-23 are vague and indefinite by reciting 'non-peptide', which are selected from peptide derivatives or analogues or peptidomimetics, wherein a single amino acid or few specific amino acids are replaced by synthetic or non-natural amino acids. However, the specification has not disclosed how many amino acids replaced and which amino acids were replaced, and further the term 'non-peptide' may read on small organic molecules which were not the peptide derivatives or peptide analogues or contain the non-natural amino acids as in applicants disclosure. Thus, the metes and bounds of the term non-peptide' is not clear.

16. Applicant's arguments filed on 9/8/05 regarding the indefinite rejection of the term 'non-peptide', have been fully considered but they are not persuasive.

Applicants traverse the rejection. Applicants assert that the present specification has defined the term 'non-peptide compound'; 'to include compounds comprising at least one

molecule other than a non-natural amino acid residue, wherein the structure of the compounds can not be determined by standard sequencing methodologies but rather must be determined by more complex chemical strategies such as mass spectrometric methods.'

Applicants assertion shave been fully considered and are not persuasive, since the definition applicants referring to only excludes the presence of natural amino acids in the non-peptide compounds, however has not recited which compounds are considered as non-peptides. The specification ha not addressed whether small organic molecules are present in the non-peptide compounds or only non-natural amino acids are present in the non-peptides. It is not clear which compounds infringe the non-peptide compounds of the claimed invention. Thus the rejection of record has been maintained.

17. Claims 1-3, 5-7, 10-16, 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lam et al (US Patent 5,650489) and Gallop et al (Journal of Medicinal Chemistry. Vol. 37, Number 9, April 1994, pages 1233-1251).

The instant claims briefly recite a method for identifying a non-peptide compound that binds to a target, the method comprising: a) forming a first library of peptides; b) selecting from the first library a family of peptides that bind to the target; c) determining the amino acid sequence of the family of peptides and generating a peptide motif; d) forming a second library comprising non-peptide compounds; e) selecting from the second library at lest one-non-peptide compounds that bind to the target; f) determining the structure of at least one non-peptide compound; g) thereby identifying the non-peptide compounds that binds the target.

Lam et al teach library of bio-oligomers of defined size and known composition, in which the library contains all of the possible sequences of the bio-oligomers, and methods of synthesis of the

library, and the bio-oligomers are peptides. And the reference methods include methods to identify bio-oligomer from the library that demonstrate the desired characteristics, such as binding (refers to the instant claim steps a-b) (i.e., see the abstract). The reference teaches that the method may be used for synthesis of random peptides as well as for synthesis of a peptide library that comprise pre-determined sequences (i.e., see column 10). The reference teaches that the method includes steps of generating a random library of peptides; contacting the library with target (acceptor); and isolating the library members which exhibit binding to the target; and sequencing the identified library members (i.e., see column 5).

Lam et al teach that the peptide libraries comprising D-amino acids, peptidomimetics, peptidomimetic bonds, and non-classical amino acids (i.e., see column 11-13). The reference teaches that the structure of the peptides comprising non-classical peptides is determined by mass spectral analysis (i.e., see column 13). The reference teaches the methods for modification or derivatization of the peptides in the library (i.e., see column 13, 14). Lam et al teach that the peptides comprising D-amino acids (non-peptides of the instant claims) will be resistant to L-amino acid-specific proteases in vivo. And the reference teaches that the modified peptide bond compounds (non-peptides) would be resistant to peptide bond hydrolysis, and such libraries would provide ligands with unique function and activity, such as extended half-lives in vivo due to resistance to metabolic breakdown or protease activity (i.e., see column 11)

The reference teaches that the bio-oligomers of interest discovered during an initial screening need not be final ligands. In fact, it is preferable to synthesize a second library based on common sequences (peptide motif) of the ligands selected during the first screening,. In this way, one may be able to identify ligands of higher activity. (i.e., see column 16, last paragraph bridging column 17).

The claimed invention differs by reciting 'forming a second library comprising non-peptide compounds, and selecting at least one non-peptide that binds to the target. Lam et al teach peptide or

peptide analog library synthesis and methods of screening the library for a ligand that binds to a target. Lam et al teach that a second library can be generated using the ligand identified during the initial screening, and advantages of the methods. Lam et al do not teach that the second library, which is based on, the ligand identified from the initial (first) library is non-peptide. However, Lam et al teach the use of D-amino acids or non-natural amino acids in the synthesis of the peptide libraries. A person skilled in the art would have been motivated to use the methods of synthesis of peptides and non-peptides taught by Lam et al to synthesize a second library based on the ligand selected from the first library, and identify the non-peptide compound which binds to the target, and determine the structure of the compound, because Lam et al teach that the method would allow to identify higher affinity or active compounds. And it would have been obvious to one skilled in the art at the time the invention was made to make multiple (or a third) library based on the non-peptide selected and screen the library for active compounds, such more diverse or higher affinity compounds would be identified.

Gaollop et al review the applications of combinatorial technologies to Drug Discovery and peptide combinatorial libraries. Gallop et al teach the building block strategy , and the number of possible different individual compounds, N, prepared depends on number of building blocks used in each step, b, and number of synthetic steps in the reaction scheme, x, Gallop et al teach the phage display peptide libraries and methods of screening for active peptides. Gallop et al teach phage display libraries of 10^7 to 10^8 recombinants. The reference teaches antibody library synthesis, and method of screening with an antigen, and in vitro affinity improvements of the large number of selected clones. The in-vitro affinity improvement is accomplished by continuing selection of the pool of antibodies, or by introducing sequence variation into the enriched antibody pool and reapplying selection (see right column in page 1236). Further the article includes combinatorial libraries using multipin synthesis, and mimotope strategy. Peptide mixtures (libraries) were synthesized using the 20 common L-amino acids, and screened for antibody binding, and the identified sequence then provides a basis for a further round of synthesis, in

which both L- and D- amino acids, non- or other amino acids are used. Thus, it was well known at the time the invention was filed to use the ligands identified in the first library as basis to synthesize a second library with non-natural amino acids and screen for improved activity ligands.

Thus a person skilled in the art would have been motivated to use the ligands (peptides) identified in the first library as basis for synthesis of non-peptide libraries because the non-peptide compounds would be useful as pharmaceuticals or in therapy since the non-peptide compounds are resistant to proteolysis and have better half-lives in vivo.

18. Applicant's arguments filed on 9/8/05, regarding the rejection of claims over Lam et al and Gallop et al, have been fully considered but they are not persuasive.

Applicants traverse the rejection. Applicants argue that examiner has failed to provide the necessary motivation to impel one of ordinary skill in the art to make Applicant's invention.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In this case Lam et al provide the motivation by teaching that the peptide libraries comprising D-amino acids, peptidomimetics, peptidomimetic bonds, and non-classical amino acids (refers to the non-peptides of the instant claims). **Lam et al further teach that the bio-oligomers of interest discovered during an initial screening need not be final ligands. In**

fact, it is preferable to synthesize a second library based on common sequences (peptide motif) of the ligands selected during the first screening. In this way, one may be able to identify ligands of higher activity. Thus, at the time the invention was made it would have been obvious to one skilled in the art to make second library based on the compounds identified from the first library.

And further the secondary reference Gallop et al teach that the Peptide mixtures (libraries) were synthesized using the 20 common L-amino acids, and screened for antibody binding, **and the identified sequence then provides a basis for a further round of synthesis, in which both L- and D- amino acids, non- or other amino acids are used.** Thus, it was well known at the time the invention was filed to use the ligands identified in the first library as basis to synthesize a second library with non-natural amino acids and screen for improved activity ligands.

Applicants argue that Lam et al do not teach forming a first library comprising a multiplicity of peptides, and selecting peptides that bind to the target, determining the sequence.

Applicants arguments have been considered and are not persuasive, since Lam et al specifically teach that the method may be used for synthesis of random peptides as well as for synthesis of a peptide library that comprise pre-determined sequences, and the method includes steps of generating a random library of peptides; contacting the library with target (acceptor); and isolating the library members which exhibit binding to the target; and sequencing the identified library members.

Examiner agrees that Lam et al do not teach the second library synthesized based on the peptide identified from the first library. However, Lam et al teach that a second library can be

prepared based on the peptides identified from the first library, and further teaches peptides comprising the D-amino acids, peptidomimetics, peptide mimetic binds, and non-classic amino acids. Thus, Lam et al provide motivation to synthesize a second library and a non-peptide library.

Applicants argue that Examiner has used applicant's invention as a blue print to combine the references.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case both the references provide ample motivation to synthesize a second library based on the peptide identified in the first library. **Lam et al further teach that the bio-oligomers of interest discovered during an initial screening need not be final ligands. In fact, it is preferable to synthesize a second library based on common sequences (peptide motif) of the ligands selected during the first screening. And the secondary reference Gallop et al teach that the Peptide mixtures (libraries) were synthesized using the 20 common L-amino acids, and screened for antibody binding, and the identified sequence then provides a basis for a further round of synthesis, in which both L- and D- amino acids, non- or other amino acids are used.**

Applicant's response refers to several case laws regarding the obviousness rejections.

However, these case laws refer to specific reagents (i.e., In re Vaeck is to the use of a specific bacterial genes) used in a method. However, in the instant case neither the references nor the claimed invention is drawn to specific products or obviousness based on the products used.

Applicants argue that 'applicants unexpected results further demonstrate that the examiner has failed to establish a prima facie case of obviousness.'

In response to applicant's argument that 'the potency of the selected non-peptide compounds was increased by 1000-fold...(an unexpected results), the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the potency of the selected non-peptide compounds was increased by 1000-fold...) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Thus for the reasons of record the rejections of record have been maintained.

19. Claims 1-7, 10-16, 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lam et al (US Patent 5,650,489) and Gallop et al (Journal of Molecular Medicine, vol. 37, no. 9, pages 1233-1251) as applied to claims 1-3, 5-7, 10-16, 21-23 above, and further in view of Benjamin et al (US Patent 6,475,806 B1) (filing date 6/7/95).

Lam and Gallop et al have been discussed supra. The claimed invention differs from the

combined teachings of Lam et al and Gallop et al, by reciting the first library is anchor library. Lam et al teach peptide or peptide analog library synthesis and methods of screening the library for a ligand that binds to a target. Gaollop et al review the applications of combinatorial technologies to Drug Discovery and peptide combinatorial libraries. Neither Lam et al , nor Gallop et al teach 'anchor library.' However, Benjamin et al teach anchor libraries and identification of peptide sequences of peptide binding sequences. The anchor library taught by Benjamin et al has same sequence as the instant specification peptide sequences. Benjamin et al teach that the anchor library is used to identify a peptide sequence that binds to the target. Thus, it would have been obvious to use the anchor libraries taught by Benjamin et al with the instant claimed method.

20. Applicant's arguments filed on 9/8/05 regarding the rejection of claims over Lam et al, Gallop et al, Benjamin et al, have been fully considered but they are not persuasive.

Applicants traverse the rejection.

The response to the traversal of the rejection of Lam et al and Gallop et al addressed supra has been incorporated by reference (see *Supra*).

Applicants argue that Benjamin et al does not make up for the deficiencies in the Lam et al and Gallop et al references.

Applicants In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicant's argument that the unexpected results, the fact that applicant has recognized another advantage, which would, flow naturally from following the suggestion of the

prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the unexpected results) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The rejections of record have been maintained for the reasons of record.

21. Claims 1-7, 10-17, and 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lam et al (US Patent 5,650,489) and Gallop et al (Journal of Molecular Medicine, vol. 37, no. 9, pages 1233-1251) as applied to claims 1-7, 10-16, 21-23 above, and further in view of Stankova et al (Drug Development Research, vol. 33, pages 146-156, 1994).

Lam and Gallop et al have been discussed supra. The claimed invention differs from the combined teachings of Lam et al and Gallop et al, by reciting the use of tandem mass spectrometry to analyze the structure of the non-peptide compound. However, Stankova et al teach the use of tandem mass spectrometry for analysis of structure of compounds identified fro a library. Thus, it would have been obvious to one skilled in the art at the time the invention was made to use tandem mass spectrometry to analyze the non-peptide compounds identified.

22. Applicant's arguments filed on 9/8/05, regarding the rejection of claims over Lam et al, Gallop t al and Stankova et al, have been fully considered but they are not persuasive.

The response to the traversal of the rejection of Lam et al and Gallop et al addressed supra has been incorporated by reference (see *Supra*).

Applicants argue that Stankova et al does not make up for the deficiencies in the Lam et al and Gallop et al references.

Applicants In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicant's argument that the unexpected results, the fact that applicant has recognized another advantages, which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the unexpected results) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The rejections of record have been maintained for the reasons of record.

23. Claims 1-7, 10-23 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-33 of copending Application No. 10/610,927. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the reference and instant claimed methods are drawn to identifying non-peptide compounds, and the reference methods only differ by reciting 'biologically generated' first library which would include phage

display library of instant claim 2; and further the reference method recites 'at least one peptide that binds to target' which is open to the instant claim method 'a family of peptides that bind to the target.'

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

24. Applicant's arguments filed on 9/8/05, regarding the provisional Obviousness-type double patenting rejection have been fully considered but they are not persuasive.

Applicants stated that 'applicants will consider submitting a terminal disclaimer in that application, which will obviate this rejection.

Applicant's assertions have been considered. However, the rejection has been maintained until a terminal disclaimer has filed and entered.

Conclusion

25. No claims are allowed.

26. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 571-272-0809. The examiner can normally be reached on Monday through Friday between 7 AM and 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Padmashri Ponnaluri
Primary Examiner
Art Unit 1639

27 November 2005

PONNALURI
PRIMARY EXAMINER